UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,606	05/23/2001	Julianna Lisziewicz	RGT 7028	2145

7590 05/26/2004

The Law Offices of Valerie E. Looper
77126 Lightfall Court
Columbia, MD 21044

EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/863,606	LISZIEWICZ ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,16 and 21-27* is/are pending in the application.

4a) Of the above claim(s) *15,16 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3-11-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 3-11-04 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-14 and 17-20 have been cancelled. Claims 15, 16, 21-27 are pending .

Election/Restrictions

This application contains claims 15, 16 and 21 drawn to an invention nonelected with traverse in the paper filed 5-12-03. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 15, 16 and 21 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Newly submitted claims 22-27 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

New claim 22 only requires administering ddI (an RT inhibitor) but not indinavir (a protease inhibitor); however, the original claims required the antiretroviral drug therapy comprised two different drugs (hydroxyurea+RT inhibitor (15) or RT inhibitor+protease inhibitor (18)). In addition, the original restriction/election was limited to administering an RT inhibitor and a protease inhibitor and the species of ddI and indinavir. Therefore,

new claim 22 is broader than the original claims and would require a new restriction based on the combination of ddI+protease inhibitor (new claim 23), ddI+a second RT inhibitor (new claim 24). The burden required to search administering ddI+any protease inhibitor or any second RT inhibitor in combination with DNA encoding an immunogenic retroviral protein would be undue.

New claim 25 only requires administering indinavir (a protease inhibitor) but not ddI (an RT inhibitor); however, the original claims required the antiretroviral drug therapy comprised two different drugs (hydroxyurea+RT inhibitor (15) or RT inhibitor+protease inhibitor (18)). The original restriction/election was limited to administering an RT inhibitor and a protease inhibitor and the species of ddI and indinavir. Therefore, new claim 25 is broader than the original claims and would require a new restriction based on the combination of indinavir+RT inhibitor (new claim 26) or indinavir+another protease inhibitor (new claim 27). The burden required to search administering Indinavir + any second protease inhibitor or any RT inhibitor in combination with DNA encoding an immunogenic retroviral protein would be undue.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, embodiments directed toward using only ddI or only indinavir in combination with DNA encoding an immunogenic retroviral protein will not be considered and have been withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicants' statement that "amended claims are generic with respect to claims 15, 16 and 21, as the latter group relates to an additional limitation that can be added to each of the above claims" is confusing and does not help to clarify how new claim 22 relates to the elected invention.

Claims 22-27 are under consideration as they relate to administering antiretroviral drug therapy comprising ddI and Indinavir until viral replication is suppressed, and then administering DNA encoding an immunogenic retroviral protein operably linked with a promoter as claimed.

The information disclosure statement filed 3-11-04 has been considered.

The response filed 3-11-04 is not in the proper format because claims 15, 16 and 21 have not been reiterated. Applicants' request for reinstatement of claims 15, 16 and 21 "as claims depending from the current set" has not been granted because the claims are not dependent upon claims 21-27.

The response filed 3-11-04 is not a proper response because it does not properly address the double patenting rejection. A proper response to a double patenting rejection is an argument, a terminal disclaimer or an indication of willingness to file a terminal disclaimer. To expedite prosecution, the office no longer accepts a request to defer a response to a double patenting rejection as an acceptable response.

Specification

The CRF has been entered and is sufficient.

The abstract filed 3-11-04 has been entered.

The first line of the specification has been updated to reflect the fact that 09/153,198 is now US Patent 6,420,176.

The status of US Patent Applications on pg 4, line 28, pg 11, line 23, and pg 16, line 29, need updated.

The status of US Patent applications on pg 21, lines 1-16 has been updated.

The headings for Fig. 8, 11, 12 and 13 on pg 7 and 8 have been corrected.

It is noted that the US patent application number on pg 21, 09/058,753 was in error and should have been 09/048,886. This is readily apparent from the title of the application. 09/048,886 has now issued as 6,251,874.

It is noted that the US patent application number on pg 21, 09/048,56, was in error and should have been 09/048,576. This is readily apparent from the title of the application. 09/048,576 has been abandoned.

The amendment filed 3-11-04 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material that is not supported by the original disclosure is as follows: the specification does not support the changes made to the paragraph bridging pg 22-23 or the paragraph bridging pg 23-24. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

New claims 22 and 25 are objected to because they do not clearly set forth the replication of the retrovirus is suppressed. While claims 22 and 25 state that the host is infected with a retrovirus and that viral replication is suppressed, the viral replication being suppressed could be any virus. The claim should more clearly state that replication of the retrovirus is suppressed.

New claims 22 and 25 are objected to because they do not clearly set forth the gene delivery complex comprises two elements, the DNA and the mannosylated polyethylenimine. The two steps may be marked i) and ii) and the two element of the gene delivery complex used in step ii) may be marked a) and b).

Claim Rejections - 35 USC § 112

Claims 22-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record.

The rejection regarding a "specific affinity for a receptor of an antigen presenting cell" has been withdrawn because the phrase has not been included in new claims 22-27.

The rejection regarding "affinity" has been withdrawn because the phrase has not been included in new claims 22-27.

The rejection regarding suppressing any viral replication using "antiretroviral drug therapy" other than retroviral replication has been withdrawn because new claims 22-27 have been limited to suppressing viral replication in a host infected with a retrovirus.

Administering an antiretroviral drug therapy comprising ddI and Indinavir until viral replication is effectively suppressed is considered enabled because Finzi taught administering a reverse transcriptase inhibitor and a protease inhibitor suppressed viral replication (Finzi et al. Science. Nov. 14, 1997, Vol. 278, pg 1295-1300).

Claims 22-27 require administering DNA encoding an immunogenic retroviral protein after administering the antiretroviral drug therapy. The sole disclosed purpose for administering DNA encoding an immunogenic retroviral protein is to induce an immune response against the retroviral protein that is therapeutic (pg 2, lines 14-19). Therefore, the step of administering DNA encoding an immunogenic retroviral protein must be fully enabled for using the DNA to obtain a therapeutic immune response against the "immunogenic retroviral protein". However, the specification does not enable using DNA encoding an immunogenic retroviral protein to induce a therapeutic immune response against a retrovirus in a host.

Claims 22-27 are not enabled because the structure of the DNA encoding an immunogenic retroviral protein that provides a therapeutic immune response against the retroviral protein is not enabled.

The state of the art at the time of filing was that the combination of vector, promoter, route of administration, level of expression and target tissue required to obtain a therapeutic or prophylactic effect using gene therapy was unpredictable. Miller

of record (1995, FASEB J., Vol. 9, pages 190-199) review the types of vectors available for *in vivo* gene therapy, and conclude that "for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances...targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated into components of safe and highly efficient delivery systems" (page 198, column 1). Deonarain of record (1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicate that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art that show promise but states that such techniques are even less efficient than viral gene delivery (see page 65, first paragraph under Conclusion section). Verma of record (Sept. 1997, Nature, Vol. 389, pages 239-242) reviews vectors known in the art for use in gene therapy and discusses problems associated with each type of vector. The teachings of Verma indicate a resolution to vector targeting has not been achieved in the art (see entire article). Verma also teaches appropriate regulatory elements may improve expression, but it is unpredictable what tissues such regulatory elements target (page 240, sentence bridging columns 2 and 3). Crystal of record (1995, Science, Vol. 270, page 404-410) also reviews various vectors known in the art and indicates, "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409).

The state of the art regarding treating retroviral infection was unpredictable. Stricker of record (Medical Hypotheses, June 1997, Vol. 48, pages 527-9) teaches that attempts to develop a vaccine against HIV have been unsuccessful because HIV vaccines do not neutralize HIV (pg 527, last paragraph through all of pg 528). Overall, a lack of understanding about protective immunity to HIV in humans, the sequence variability of HIV and the rapid replication of HIV contribute the ineffectiveness of vaccines against HIV (Bangham of record, Nov. 29, 1997, Lancet, Vol. 350, pages 1617-1621; page 1617, top of col. 1).

The specification teaches a complex comprising i) manosylated PEI and ii) DNA encoding an immunogenic HIV protein operably linked to a promoter. Administration of the complex to a host after drug therapy was followed by an increase in CD4 cells then a decrease in CD4 cells (pg 53).

The specification does not provide adequate guidance for one of skill to use DNA encoding an "immunogenic retroviral protein" to induce an immune response capable of treating a retroviral infection. The results described in the specification are not considered therapeutic because the overall result does not result in a net increase in CD4 cells. In addition, it cannot be concluded that the DNA encoding a retroviral protein caused the initial increase in CD4 cells because the experiment did not include controls - animals that did not receive drug therapy or the gene complex. The specification does not provide adequate guidance indicating the increase in CD4 was caused by an immune response to the retroviral protein encoded by the DNA - the drug therapy could have caused the increase in CD4. The specification did not teach treating animals that

were already infected or challenging the animals after they were given DermaVir. For administration of DNA encoding a retroviral protein to induce a therapeutic immune response, the specification must overcome the unpredictability in the art by adequately describing the structure of the "foreign genetic material" used, the dosage and route of administration that results in a therapeutic effect or "immunization." Without such guidance it would require one of skill in the art undue experimentation to overcome the unpredictability in the art regarding gene therapy and retroviral therapy to determine the combination of elements required to obtain a therapeutic or prophylactic effect against retroviral infection using "foreign genetic material. Therefore, the specification does not enable "therapeutic genetic immunization" using a gene delivery complex comprising "foreign genetic material" as claimed.

Applicants have not addressed this rejection.

Claims 1-14 and 17-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection regarding claim 1 because the antiretroviral drug therapy and gene delivery complex are not administered to a host that is infected with a retrovirus has been withdrawn because the claim has been canceled.

The rejection regarding claim 1 because antiretroviral drug therapy does not suppress and "viral replication" as claimed.

The rejection regarding "effectively" in claim 1 has been withdrawn because the claim has been canceled.

The rejection regarding "foreign" in claim 1-6 has been withdrawn because the claims have been canceled.

The rejection regarding how "foreign genetic material" relates to the "non-viral vector" (claim 1) has been withdrawn because the claim has been canceled.

The rejection regarding the term "specific affinity" has been withdrawn because the claim has been canceled.

The rejection regarding a "gene delivery complex" that has an affinity for a receptor on an antigen-presenting cell has been withdrawn because the claim has been canceled.

The rejection regarding "reverse-transcriptase dependent virus" in claim 3 has been withdrawn because the claim has been canceled.

The rejection regarding a "substantial portion" of a replication defective HIV (claim 4-6) has been withdrawn because the claims have been canceled.

The rejection regarding "an integrase negative mutant of a dual-tropic primary isolate of a human immunodeficiency virus" (claim 6) has been withdrawn because the claim has been canceled.

The rejection regarding the phrase "the reading frames of the integrase gene" in claim 7 has been withdrawn because the claim has been canceled.

The rejection regarding claim 8 being unclear has been withdrawn because the claim has been canceled.

The rejection regarding the phrase "complex is DNA and one or more agents" (claim 8) has been withdrawn because the claim has been canceled.

The rejection regarding claim 8 and the Markush Group being improper has been withdrawn because the claim has been canceled.

The rejection regarding claim 9 because "sugar-modified polyethylenimine" does not clearly set forth the structure of the agent has been withdrawn because the claim has been canceled.

The rejection regarding claim 10 because it is unclear if glucose is further limiting the "sugars" or the "derivatives" of PEI in claim 8 has been withdrawn because the claim has been canceled.

The rejection regarding the phrase "antiretroviral drug combination" in claim 17 has been withdrawn because the claim has been canceled.

The rejection regarding "highly active" antiretroviral drug therapy (claim 17) has been withdrawn because the claim has been canceled.

The rejection regarding the Markush format of claims 18 and 20 has been withdrawn because the claims have been canceled.

The rejection of claims 19 and 20 as having the trademark/trade name delavirdine, abacavir, adefovir, nevirapine, efavirenz, lubocavir, PMPA, PMEA, indinavir, saquinavir, ritonavir, nelfinavir, and GW41, has been withdrawn because the claims have been canceled.

Claims 22-27 are free of the prior art as they relate to the elected invention. The prior art did not teach or suggest administering ddI and Indinavir until viral replication is effectively suppressed, and then administering a gene delivery complex as claimed. Finzi (Science. Nov. 14, 1997, Vol. 278, pg 1295-1300) taught administering reverse transcriptase inhibitors and protease inhibitors to HIV patients. However, Finzi did not relate to administering DNA encoding the marker protein luciferase to the brain of mice as taught by Boussif (PNAS, Aug. 1995, Vol. 92. pg 7292-7301) of record, administering DNA encoding a marker protein to cells *in vitro* as taught by Zanta (Bioconjugate Chem. 1997. Vol. 8. pg 839-844) of record, administering DNA encoding a marker protein to cells *in vitro* as taught by Behr (US Patent 6,013,240) of record, or administering virus encoding integrase-defective HIV to cells *in vitro* as taught by Cara (Virology, 1995, Vol. 208, pg 242-248).

The following references have also been reviewed again:

Lori, Science, 1994, Vol. 266, pg 801-805;

Lori, AIDS Res. Hum. Retrovir., 1997. Vol. 13, pg 1403-1409;

Lori, AIDS Res. Hum. Retrovir., 1995, Vol. 11, pg 1149-1151;

Hollinshead, US Patent 5,747,526;

Malley US Patent 5,521,161;

Malley, US Patent 5,736,526;

Lin, US Patent 5,719,132;

Lori, US Patent 6,046,175 ;

Malley, US Patent 6,093,702 ;

Lori, US Patent 6,194,390 ;

Critchfield, US Patent 6,274,611;

Lisziewicz, US Patent 6,114,312;

Lisziewicz, US Patent 6,251,874;

Lisziewicz, US Patent 5,977,086.

Double Patenting

The rejection regarding the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,130,089 in view of the disclosure of 6,130,089 has been withdrawn in view of applicants' arguments.

Claims 22-27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,420,176 in view of the disclosure of 6,420,176 for reasons of record. The claims of '176 are directed toward a gene delivery complex comprising DNA encoding an immunogenic protein operably linked to a promoter and monosylated polyethylenimine. The claims of '176 do not require administration as required in the instant claims or administration of antiretroviral drug therapy. MPEP 804 states the specification may be used as a dictionary to learn the meaning of a term in the patent claim. In this case, one of skill would look to the specification to determine the asserted utility of the product. The disclosure taught administering the gene delivery complex after suppressing viral replication using antiretroviral drug therapy (col. 12, lines 11-51, see especially lines 20-27). Thus, it would have been obvious to one of ordinary skill in

the art at the time the invention was made to administer the gene delivery complex in combination with drug therapy as claimed. Applicants request to defer response will not be acceptable in any future response.

Claims 22-27 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application No. 10/081922 for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because they overlap in scope. Applicants request to defer response will not be acceptable in any future response.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at 571-272-0738.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER